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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/921,060	08/29/97	ANDERSON	D 012712-432

HM22/1024

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EXAMINER	
SCHWADRON, R	
ART UNIT	**PAPER NUMBER**
1644	28

DATE MAILED: 10/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

US GPO 2000; 465-188/25268

Office Action Summary

Application No.	Applicant(s)
08/921,060	Anderson et al.
Examiner	**Group Art Unit**
Ron Schwadron, Ph.D.	1644

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *11-15* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *11-15* is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. The request filed on 8/9/2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/921060 is acceptable and a CPA has been established. An action on the CPA follows.

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because It does not identify the citizenship of each inventor. The citizenship of Inventors Hanna and Newman has been omitted.

Applicant has indicated that a new oath will be provided upon indication of allowance.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title should indicate that the invention involves treatment of B cell lymphoma with anti-CD20 antibody and at least one chemotherapeutic agent.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "dosage of about .4 mg/kg" in claim 11. While the specification discloses the claimed method using about .4 mg/kg to about 20 mg/kg body weight of antibody, it does not disclose the claimed method wherein no upper limit is specified. Regarding applicants comments in page 9 of the amendment

filed 2/1/2000, the particular passages of the specification to which applicant refers disclose use of about .4 mg/kg to about 20 mg/kg body weight of antibody, it does not disclose the claimed method wherein no upper limit is specified. The scope of the written description provided in the specification is not commensurate with the scope of the claimed invention.

This rejection was discussed with SPE Chan.

6. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "from 0.4 to about 20" in claim 12 lacks antecedent basis in claim 11 which recites "about 0.4".

7. Regarding applicants comments about priority for the claimed invention, the following comments are made. While there is support in the instant application for the method of claims 11-13 (eg. original claims 8-10), there is no support for the claimed invention in pages 15 and 16, and pages 61-62 of the instant specification or in said pages of the specification of 08/149099. Original claims 8-10 were not present in parent application 08/149099 (now US Patent 5,736,137). Regarding columns 30-32 of US Patent 5,736,137 (eg. pages 61-62 of 08/149099), said passages of the specification disclose the use of C2B8 in combination with a therapeutic agent, but do not disclose the scope of the invention of claims 11-13 (eg. use of the antibody recited in section (I) of claim 11). The claimed invention is not disclosed in said passage, because said passage is restricted to the disclosure of the use of C2B8 in combination with a chemotherapeutic agent. There is also no disclosure in application 08/149099 of the claimed invention using C2B8 and "at least one chemotherapeutic agent". There is no disclosure in the parent application of the claimed method that uses a mixture of the chemotherapeutic agents recited in said claim in combination with C2B8.

This issue was discussed with BPS Schwartz on 7/13/99.

Regarding applicants comments about column 32 of US Patent 5,736,137, said column does not disclose or incorporate by reference use of a mixture of chemotherapeutic agents. The material incorporated by reference in column 32 refers to use of the individual agents recited in lines 5-7, not mixtures of said agents.

8. Claims 11-15 are rejected under 35 U.S.C. § 102(e) as being anticipated by Anderson et al. (US Patent 5,736,137).

Regarding the inventors of US Patent 5,736,137, the inventorship is incorrectly listed on said patent. John Leonard was removed as an inventor of said application (see Paper 39 of 08/149099, also see inventors listed on file jacket of said application). Thus, US Patent 5,736,137 constitutes prior art under 35 U.S.C. § 102(e). Anderson et al. teach the use of C2B8 (a particular species of anti-CD20 therapeutic antibody) in combination with a chemotherapeutic agent wherein the agent is administered, as per the times recited in the claims, wherein the agent is one of the agents recited in claim 15.

Applicant has requested that this rejection be held in abeyance pending the submission of a declaration that would change the inventorship in the instant application such that US Patent 5,736,137 would not constitute prior art.

9. Claim 11 is rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kaminski et al. (US Patent 5,595,721).

Kaminski et al. teach the use of a chimeric anti-CD20 antibody for the treatment of B cell lymphoma(see column 7). Kaminski et al. teach the administration of therapeutic anti-CD20 antibody in combination with cyclophosphamide (see column 33). Kaminski et al. teach that said antibody causes apoptosis of cells which are bound by said antibody (see column 33). While Kaminski et al., do not teach that this antibody has the functional characteristics recited in claim 11, part (I), it appears that said characteristics would be found in an antibody that induces apoptosis when bound to target cells. Therefore the claimed method appears to be same or similar to the method of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the method of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the method of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

Regarding applicants comments as they apply to this rejection, Kaminski et al. teach the use of a chimeric anti-CD20 antibody for the treatment of B cell lymphoma(see column 7). Regarding applicants comments about the disclosure of Kaminski et al., as applicant is well aware, there is no requirement that a specific example of an invention be present in order for the

disclosure to be enabled. Kaminski et al. teach that said antibody causes apoptosis of cells which are bound by said antibody (see column 33). There has been no evidence provided that the antibody disclosed by Kaminski et al. (eg. chimeric B1 antiCD20 antibody) does not have the property of causing apoptosis of cells which are bound by said antibody. Therefore, the disclosure of Kaminski et al. is presumed to be enabled. While Kaminski et al., do not teach that this antibody has the functional characteristics recited in claim 11, part (I), it appears that said characteristics would be found in an antibody that induces apoptosis when bound to target cells. Therefore the claimed method appears to be same or similar to the method of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the method of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the method of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Regarding applicants comments about nonobviousness, while Kaminski et al., do not teach that this antibody has the functional characteristics recited in claim 11, part (I), it appears that said characteristics would be found in an antibody that induces apoptosis when bound to target cells. Regarding applicants comments about parent application 08/149099, the claims of said application are drawn to a particular species of antibody (eg. C2B8) not recited in the claim rejected in this rejection.

9. Claims 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Press et al. (Blood) in view of Hellstrom et al. (WO 92/07466) and Robinson et al. (US Patent 5,500,362).

Press et al. teach the use of a murine anti-CD20 antibody (see abstract) for the treatment of B cell lymphoma. Press et al. teach that therapeutic anti-CD20 antibody was administered to patients that had received at least one chemotherapeutic agent(see page 586, column 1). Press et al. teach the use of murine anti-CD20 antibody wherein said antibody depletes virtually all peripheral B cells within 24 hours(see Figure 2) wherein the dosage used is encompassed by the range recited in claim 11 (see Figure 2). Press et al. does not teach that the method uses a chimeric antibody with the functional property recited in the claims. While the murine antibody taught by Press et al. has the functional properties recited in claim 11, Robinson et al. teach that it would be expected that a chimeric anti-CD20 would have greater lytic activity in vivo compared to the murine antibody from which it is derived, because the chimeric antibody would possess

increased ADCC and CDC (see column 20). Hellstrom et al. teach that chimeric antibodies have increased immune function because they contain human Fc (see page 13). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Press et al. teaches the use of antiCD20 antibody to treat B cell lymphoma, while Hellstrom et al. teach chimeric monoclonal antibody treatment in combination with chemotherapeutic agents can be used to treat cancer and both Hellstrom et al. and Robinson et al. teach the use of chimeric antiCD20 antibody to treat B cell lymphoma and the advantages of using such antibodies. One of ordinary skill in the art would have been motivated to do the aforementioned because Hellstrom et al. teach the use of chimeric antibodies in combination with chemotherapy (see page 7) and Robinson et al. teach the use of chimeric anti-CD20 antibody for the treatment of B cell lymphoma (see column 20). A routineer would have determined the particular time points for administering the antibody as recited in claims by routine experimentation.

Regarding applicants comments as they apply to this rejection, Press et al. (Blood) teach the use of murine anti-CD20 antibody wherein said antibody depletes virtually all peripheral B cells within 24 hours(see Figure 2) wherein the dosage used is encompassed by the range recited in claim 11 (see Figure 2). Press et al. does not teach that the method uses a chimeric antibody with the dose recited in the claims. While the murine antibody taught by Press et al. has the functional properties recited in claim 11, Robinson et al. teach that it would be expected that a chimeric anti-CD20 would have greater lytic activity in vivo compared to the murine antibody from which it is derived, because the chimeric antibody would possess increased ADCC and CDC (see column 20). Hellstrom et al. teach that chimeric antibodies have increased immune function because they contain human Fc (see page 13). Regarding applicants comments about the Anderson declaration, said declaration is drawn to the C2B8 antibody. Said antibody is not recited in the claims under consideration. The scope of the alleged unexpected results in the Anderson declaration is not commensurate with the scope of the claimed invention. Furthermore, Press et al. (Blood) teach the use of murine anti-CD20 antibody wherein said antibody depletes virtually all peripheral B cells within 24 hours(see Figure 2) wherein the dosage used (10 mg/kg) is encompassed by the dosage (eg. about .4 mg/kg) recited in claim 11 (see Figure 2). In addition, pending claim 12 indicates that about .4mg/kg encompasses the range of .4mg/kg to about 20 mg/kg. While the murine antibody taught by Press et al. has the functional properties recited in

claim 11, Robinson et al. teach that it would be expected that a chimeric anti-CD20 would have even greater lytic activity in vivo compared to the murine antibody from which it is derived, because of increased ADCC and CDC.

10. Claims 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellstrom et al. (WO 92/07466) in view of Robinson et al. (US Patent 5,500,362), Reff et al. (J. Cell. Biochem.) or Reff et al. (Blood) or Anderson et al.

Hellstrom et al. teach that monoclonal antibody treatment in combination with chemotherapeutic agents can be used to treat cancer (see page 4). Hellstrom et al. teach the use of chimeric antibodies in combination with chemotherapy (see page 7). Hellstrom et al. teach that the antibody used in the aforementioned method binds tumor cells. Robinson et al. teach the use of chimeric anti-CD20 antibody treat B cell lymphoma. Hellstrom et al. do not teach that the use of chimeric antiCD20 antibody C2B8 in said method. Reff et al. (J. Cell. Biochem.) teach the chimeric antiCD20 antibody C2B8 and that said antibody binds B cell lymphomas (see entire document). Reff et al.(Blood) teach the chimeric antiCD20 antibody C2B8 and that said antibody binds B cell lymphomas (see entire document). Anderson et al. teach the chimeric antiCD20 antibody C2B8 and that said antibody binds B cell lymphomas (see entire document). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Hellstrom et al. teach that monoclonal antibody treatment in combination with chemotherapeutic agents can be used to treat cancer wherein the antibody used in the aforementioned method binds tumor cells, Robinson et al. teach the use of chimeric antiCD20 antibodies to treat B cell lymphoma, while Reff et al. (Blood) or Reff et al. (J. Cell. Biochem.) or Anderson et al. teach chimeric antiCD20 antibody C2B8 and that said antibody binds B cell lymphomas. One of ordinary skill in the art would have been motivated to do the aforementioned because Hellstrom et al. teach that the aforementioned method can be practiced with antibody that binds tumor cells. In addition, the Reff et al. or Anderson et al. references teach that C2B8 could be used to treat B cell lymphoma. A routineer would have determined the particular time points for administering the antibody as recited in claims by routine experimentation.

Applicants comments about priority for the claimed inventions are addressed in paragraph 7 of this Office action. Regarding applicants comments about Anderson et al., Anderson et al.

refers to the Anderson et al. reference disclosed in the PTO-1449 filed 8/29/97 (eg. the 1991 Abstract). It is noted that the Anderson et al. patent, when cited in rejections in the previous Office Action is referred to as Anderson et al. (US Patent 5,736,137). Anderson et al. was published in 1991. Even if the claimed invention had priority to parent application 08/149099, the claimed inventions are not disclosed in parent application 07/978891. Therefore, the Katz type Anderson declaration filed in the instant amendment would not overcome said reference as prior art. Regarding applicants about unexpected results, the C2B8 antibody was known in the art as per the Reff et al. (J. Cell. Biochem.) or Reff et al. (Blood) or Anderson et al. references.

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

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